IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENETIC TECHNOLOGIES LIMITED, Plaintiff, v. LABORATORY CORPORATION OF AMERICA HOLDINGS, LABORATORY CORPORATION OF AMERICA, AND 23ANDME, INC., Defendants.	)	Civil Action No. 1:12-cv-01736-LPS

PLAINTIFF GENETIC TECHNOLOGIES LIMITED'S ANSWERING BRIEF IN OPPOSITION TO DEFENDANTS' MOTION TO DISMISS

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Raymond H. Lemisch, Esquire (No. 4204)
BENESCH, FRIEDLANDER, COPLAN & ARONOFF LLP
222 Delaware Avenue, Suite 801
Wilmington, DE 19801
(302) 442-7008 Telephone
(302) 442-7012 Facsimile
rlemisch@beneschlaw.com

- and –

Robert R. Brunelli, Esquire
Benjamin B. Lieb, Esquire
SHERIDAN ROSS P.C.
1560 Broadway, Suite 1200
Denver, Colorado 80202
303-863-9700 Telephone
303-863-0223 Facsimile
blieb@sheridanross.com
rbrunelli@sheridanross.com

Attorneys for Plaintiff, Genetic Technologies Limited

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I. PROCEDURAL AND FACTUAL BACKGROUND

A. GTG'S COMPLAINT AND THE '342 PATENT

Genetic Technologies Limited's ("GTG") Complaint [D.I. 1] alleges that Defendants Laboratory Corporation of America Holdings, Laboratory Corporation of America, and 23andMe, Inc.'s (collectively "Defendants") infringe one or more claims of U.S. Patent No. 7,615,342 ("the '342 Patent") through their making, using, selling, and/or offering to sell genotyping services. [*Id.* at ¶¶ 21-26.] GTG's Complaint recites "[w]ithout limitation as to claims to be asserted in this action and for exemplary purposes only," Claim 1 of the '342 Patent, which reads:

> 1. A method to predict potential sprinting, strength, or power performance in a human comprising:
> a) analyzing a sample obtained from the human for the presence of one or more genetic variations in α-actinin-3 (ACTN3) gene;
> b) detecting the presence of two 577R alleles at the loci encoding amino acid number 577 of the α-actinin-3 (ACTN3) protein; and
> c) predicting the potential sprinting, strength, or power performance of the human, wherein the presence of two copies of the 577R allele is positively associated with potential sprinting, strength, or power performance.

[D.I. 1 at ¶ 13.]

Other exemplary Claims 4, 6 and 9 of the '342 Patent read:

> 4. The method of claim 3, wherein the amount of ACTN3 protein is measured using an antibody specific for ACTN3 protein.

> 6. The method of claim 1, further comprising identifying the 577R alleles in the human's genomic DNA by DNA sequencing, allele-specific hybridization, allele-specific amplification or restriction fragment length polymorphism analysis.

> 9. A method of selecting a training program based on potential sprinting, strength, or power performance for a human comprising:
> a) analyzing a sample obtained from the human for the presence of one or more genetic variations in α-actinin-3 (ACTN3) gene;
> b) detecting the presence of two 577 R alleles at the loci encoding amino acid number 577 of the α-actinin-3 (ACTN3) protein;

> c) predicting the potential springing, strength, or power performance of the human, wherein the presence of two 577R alleles is positively associated with potential sprinting, strength, or power performance, and
>
> d) selecting a training program based on predicting potential sprinting, strength and power performance of step c).

['342 Patent, D.I. 1, Ex. A at 30:1-24.]

On February 25, Defendants filed their Motion to Dismiss, seeking dismissal of GTG's Complaint *with prejudice* on the grounds that the '342 Patent allegedly claims merely a law of nature and is thus patent ineligible under 35 U.S.C. § 101. [D.I. 9, p. 8 (the "Motion").] In fact, the '342 Patent does not claim a law of nature, but rather claims methods of utilizing the presence of the ACTN3 genotype to make predictions of an individual's athletic potential, and selecting and matching a sport or sporting event to the individual. [Declaration of Maria Luisa Ashdown ("Luisa Dec."), Ex. A at ¶ 4.]

The '342 Patent specification describes that "α-actinins play a role in thin filament organization and the interaction between the sarcomere cytoskeleton and the muscle membrane[,]" and that α-actinins further play "a role in the regulation of myofiber differentiation and/contraction." [*Id.* at 2:27-38.] Additionally, the '342 Patent describes the apparent functional redundancy of the α-actinin-2 gene (ACTN2) and the α-actinin-3 gene (ACTN3) and the hypothesis "that [ACTN2] is able to compensate for the absence of [ACTN3] in type 2 (fast) fibers in humans." [*Id.* at 2:54-67.] Despite this functional redundancy, the '342 Patent describes that there is "a very low frequency of homozygosity for the ACTN3 premature stop codon 577X mutation" in elite athletes (particularly sprinters, swimmers, and cyclists) as compared to the general Caucasian population." [*Id.* at 3:3-15.]

In turn, the Abstract describes the inventive methods of the '342 Patent:

> The present invention concerns novel methods of selecting or matching a sport or sporting event to an individual (e.g. a sprint/power sport or an endurance sport)

> and predicting athletic performance, the methods involving assessing ACTN3 genotype. In alternative embodiments, training regimens may be optimally designed for athletes by assessing the ACTN3 genotypes. Certain embodiments concern combining the assessment of the ACTN3 genotype with other known fitness related genes to better assess the athletic potential of an individual. In addition, the genotypic analysis of the ACTN3 gene may be combined with physiological tests, physical measurements and/or psychological assessments to more optimally design a training regimen for an individual athlete.

[D.I. 1, Ex. A at p. 1.]

B. PATENTABILITY UNDER 35 U.S.C. § 101

The Supreme Court recently addressed the scope of patent eligible subject matter under 35 U.S.C. § 101 in *Mayo Collaborative Servs. v. Prometheus Labs., Inc.* wherein it considered claims directed to the use of thiopurine to treat autoimmune diseases. 132 S. Ct. 1289 (2012). The claims at issue in *Mayo* recited two steps – an "administering" step and a "determining" step. *Id.* at 1297-98. The administering step required administration of 6-thioguanine to a subject with autoimmune disease. *See id.* at 1295. The determining step then required determination of the metabolite level of the drug in the subject's blood, and contained a "wherein" clause describing the ideal level of 6-thioguanine in the blood. *Id.* at 1297-98. The Supreme Court found the correlation between the naturally-produced metabolites and therapeutic efficacy and toxicity to be an unpatentable "natural law" and that the two claimed steps were not genuine applications of those laws, but rather drafting efforts designed to monopolize the correlations. *See id.* In so finding, the Supreme Court noted that unlike "a typical patent on a new drug or a new way of using an existing drug, the patent claims do not confine their reach to particular applications of those laws" so as to not tie up the patent from future use of the law of nature. *Id.* at 1302.

Following the decision in *Mayo*, the Federal Circuit considered the patent eligibility of claims reciting "a method for screening a tumor sample, by comparing a first BRCA1 sequence from a tumor sample and a second BRAC1 sequence from a non-tumor sample, wherein the

difference in sequence indicates an alteration in the tumor sample." *Ass'n for Molecular Pathology v. USPTO (Myriad)*, 689 F.3d 1303, 1334 (Fed. Cir. 2012) (internal quotations omitted), *cert. granted on other grounds sub nom. Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 132 S. Ct. 694 (2012). The Federal Circuit found the claims to comparing and analyzing two genetic sequences were an abstract mental process and not patent eligible under 35 U.S.C. § 101. *Id.* Importantly, the Federal Circuit noted that "Myriad's claims do not apply the step of comparing two nucleotide sequences in a process. Rather, the step of comparing two DNA sequences is the entire process that is claimed." *Id.* at 1334-35.

The Federal Circuit in *Myriad*, however, did uphold the patent eligibility of a claim using host cells to transform an altered BRCA1 gene in the presence of a potential cancer therapeutic or in the absence of the therapeutic, explaining that those "cells, like the patent-eligible cells in *Chakrabarty*, are not naturally occurring. Rather, they are derived by altering a cell to include a foreign gene, resulting in a man-made transformed cell with enhanced function and utility." *Myriad*, 689 F.3d at 1336. Thus the claim was patentable because it "applies certain steps to transformed cells that . . . are a product of man, not nature." *Id.* The *Myriad* court also upheld the patentability of composition claims directed to isolated DNA. The court found that these composition claims were patent eligible because "the claims cover molecules that are markedly different – having a distinctive chemical structure and identity – from those found in nature." *Id.* at 1328.

Following its ruling in *Myriad*, the Federal Circuit in *PerkinElmer, Inc. v. Intema Ltd.*, considered the patent eligibility of claims directed to a method for determining whether a pregnant woman has an increased risk of having a fetus with Down's syndrome. No. 2011-1577, 2012 U.S. App. LEXIS 23845 (Fed. Cir. Nov. 20, 2012). The claimed method comprised the steps

of "measuring" the level of markers from a first and second semester screening, assaying the samples and "determining the risk of Down's syndrome by comparing the measured levels of both the [first marker] and the [second marker] with observed relative frequency distributions of marker levels in Down's syndrome pregnancies and in unaffected pregnancies." *Id.* at *2-3.[1] The Federal Circuit noted that neither the measuring steps nor the determining steps were sufficient to confer patentability because "as in *Mayo*, there is *no requirement that a doctor act* on the calculated risk. There is at most 'a suggestion' that the doctor take the mental determination into account when assessing the patent." *Id.* at *16 (emphasis added).

II. ARGUMENT

A. Legal Standard Of Review For Defendants' Motion To Dismiss

Defendants fail to disclose the procedural rule under which they seek dismissal of GTG's Complaint, but their Motion is necessarily a motion pursuant to Fed. R. Civ. P. 12(b)(6).[2] The Third Circuit employs a two-part analysis for such a motion. *Fowler v. UPMC Shadyside*, 578 F.3d 203, 210 (3rd Cir. 2009). First, the factual and legal elements of a claim are separated and the Court must "accept all of the complaint's well-pleaded facts as true, but may disregard any legal conclusions." *Id.* at 210-11. Second, the Court "must then determine whether the facts alleged in the complaint are sufficient to show that the plaintiff has a plausible claim for relief." *Id.* at 211 (quoting *Ashcroft v. Iqbal*, 556 U.S. 662, 679 (U.S. 2009) (internal quotations omitted)). "In deciding a Rule 12(b)(6) motion, a court must consider only the complaint, exhibits attached to the complaint, matters of public record, as well as undisputedly authentic documents if the complainant's claims are based upon these documents." *Mayer v. Belichick*,

[1] Defendants incorrectly assert that the claims at issue in *PerkinElmer* include a "suggesting" step. [Motion, p. 7.] There is no such limitation. *See PerkinElmer*, 2012 U.S. App. LEXIS 23845 at *2-5.

[2] Fed. R. Civ. P. 12(c) is inapplicable because Defendants have not yet answered GTG's Complaint.

605 F.3d 223, 230 (3d Cir. 2010). However, where as here, "matters outside the pleadings are presented to and not excluded by the court, the motion must be treated as one for summary judgment under Rule 56." Fed. R. Civ. P. 12(d).

As further explained below, Defendants' Motion includes factual assertions but without any evidentiary support. The Motion thus fails to satisfy Rule 56. *Supinski v. UPS*, 413 Fed. Appx. 536, 539 (3rd Cir. Pa. 2011) ("Where the moving party seeks summary judgment on an issue on which it will bear the burden of proof at trial, it must show that it has produced enough evidence to support the findings of fact necessary to win.") (internal quotations omitted).

B. Legal Standard Of Review Under 35 U.S.C. § 101

Defendants falsely assert that "patentable subject matter is a pure question of law measured by the four corners of the patent and not dependent on any subsidiary factual determinations." [Motion, p. 2.] Even the cases Defendants cite for this false assertion demonstrate that patent eligibility requires consideration of numerous factual issues outside of the patent itself. *DealerTrack, Inc. v. Huber*, 674 F.3d 1315, 1333-34 (Fed. Cir. 2012) (making the factual determination that computer-aided claims require no specific application or particular machine); *CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1376-77 (Fed. Cir. 2011) (making the factual determination that all steps of the patented process could be performed by the human mind); *In re Comiskey*, 554 F.3d 967, 975 (Fed. Cir. 2009) (acknowledging that while Appellant did not identify any relevant fact issues that must be resolved in order to address the patentability of the subject matter, "there may be cases in which *the legal question as to patentable subject matter may turn on subsidiary factual issues*") (emphasis added); *In re Bilski*, 545 F.3d 943, 963-64 (Fed. Cir. 2008) (making the factual determination that the exchange of options to purchase commodities equates to the exchange of legal obligations); *Cardpool, Inc. v. Plastic Jungle, Inc.*, No. C 12-04182 WHA, 2013 U.S. Dist. LEXIS 9280, at *4-5 (N.D. Cal. Jan.

22, 2013) (making factual determinations regarding whether steps of claim can be performed using a computer); *CyberFone Sys., LLC v. Cellco P'ship*, C.A. No. 11-827-SLR, 885 F. Supp. 2d, 2012 U.S. Dist. LEXIS 115740, at *16-22 (D. Del. Aug. 16, 2012) (making factual determinations regarding whether data processing and collection algorithms made requisite transformation to satisfy machine-or-transformation-test).

"Whether a claim is directed to statutory subject matter is a question of law. Although determination of this question may require findings of underlying facts specific to the particular subject matter and its mode of claiming. . . ." *Arrhythmia Research Tech. v. Corazonix Corp.*, 958 F.2d 1053, 1055-56 (Fed. Cir. 1992). Further, "[a] patent shall be presumed valid. . . . The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity." 35 U.S.C. § 282. To overcome this presumption, Defendants bear both the burden of persuasion and the burden of proof to establish that the '342 Patent is invalid by clear and convincing evidence. *See Microsoft Corp. v. i4i Ltd. P'ship*, 131 S. Ct. 2238, 2245, 2248 n.7 (2011). As explained below, Defendants' Motion does not satisfy this burden.

C. Defendants' Motion Is Fatally Deficient And Must Be Denied

There are at least three fatal deficiencies in Defendants' Motion.

1. Defendants' Motion Lacks Necessary Evidentiary Support

Defendants have failed to submit evidentiary support for at least the following factual assertions:

- that "taking a sample of something and analyzing it, without more, are 'conventional steps, specified at a high level of generality'" [Motion, p. 4];
- that the presence of two copies of the 577R allele is positively associated with potential sprinting, strength, or power performance "merely involves a discovery of a fact about the world" [*Id.*, pp. 4-5 and p. 8];

- that the "discovery of the relationship between the presence of the 577R allele and sprinting is an unprotectable fact about the world regardless whether the naturally-occurring allele is a SNP or not." [*Id.*, p. 8 n.3];

- that the analysis methods in Claim 6 are "each . . . well-known in the art." [*Id.*];

- that Claim 1 of the '342 Patent "does not even include *routine* additional steps" [*Id.*, p. 5 (emphasis added)]; and

- that "predicting" is "something that can be done in the human mind and that does not transform or change the outside world in any tangible way." [*Id.*]

All of these assertions are, as conceded by Defendants' arguments, necessary factual predicates to the Motion. However, conclusory statements do not satisfy Defendants' high burdens of persuasion or proof. For this reason alone, the Court must deny the Motion.

2. <u>The Asserted Claims Have Not Yet Been Determined</u>

By seeking dismissal of GTG's Complaint with prejudice [Motion, p. 8], Defendants necessarily seek a ruling that all claims of the '342 Patent are patent ineligible.[3] Such a ruling would be improper because a case or controversy does not exist for all claims of the '342 Patent. "The existence of a case or controversy must be evaluated on a claim-by-claim basis." *Fox Group, Inc. v. Cree, Inc.*, 700 F.3d 1300, 1307 (Fed. Cir. 2012) (quoting *Jervis B. Webb Co. v. So. Sys., Inc.*, 742 F.2d 1388, 1399 (Fed. Cir. 1984)). Further, "[j]urisdiction must exist at all stages of review, not merely at the time the complaint [was] filed, . . . a counterclaimant must

[3] Defendants allege, however, that only Claim 1 is asserted in this action. [Motion, p. 1.] However, GTG clearly states in its Claim for Relief that Defendants have "manufactured, made, had made, used, practiced, imported, provided, supplied, distributed, sold, and/or offered for sale genotyping services that infringe *one or more claims* of the '342 Patent in violation of 35 U.S.C. § 271(a), has performed all the steps of one or more methods claimed in the '342 Patent personally and through its direction or control [of the other Defendant] in violation of 35 U.S.C. § 271(a), and/or has induced direct infringement of the '342 Patent by others . . ., by having actively instructed, assisted and/or encouraged others to practice one or more of the inventions claimed in the '342 Patent in violation of 35 U.S.C. § 271(b)." [Complaint, D.I. 1, ¶¶ 22, 25 (emphasis added)]; *cf. Rmail LTD. v. Right Signature, LLC*, No. 2:11-cv-300, 2012 U.S. Dist. LEXIS 92932, at *5 (E.D. Tex. Jul. 5, 2012) ("Plaintiffs are not required to identify specific claims or claim elements at [the initial] stage of litigation."); Fed. R. Civ. P. 84, Form 18.

show a continuing case or controversy with respect to withdrawn or otherwise unasserted claims." *Id.* (quoting *Streck, Inc. v. Research & Diagnostic Sys., Inc*., 665 F.3d 1269, 1282-83 (Fed. Cir. 2012)). In *Fox Group*, the Federal Circuit vacated a district court's ruling that all claims of the patent-in-suit were invalid because the district court did not have jurisdiction over the unasserted claims of the patents-in-suit. In *Streck*, the Federal Circuit held that the district court only had jurisdiction over the claims of the patents-in-suit that the patentee had asserted in its infringement contentions because no case or controversy existed as to the other claims. Here, the claims at issue have not yet been identified. Thus, at this stage, the Court lacks jurisdiction to decide that the entire '342 Patent is invalid. *Fox Group*, 700 F.3d at 1307. The Motion is premature and must be denied for this reason as well.

3. Claim Construction is Required

Once the asserted claims are determined, they will require construction before any patent eligibility analysis. Claim construction "is an important first step in a § 101 analysis." *In re Bilski*, 545 F.3d at 951 (en banc) (citing *State St. Bank & Trust Co. v. Signature Fin. Group*, 149 F.3d 1368, 1370 (Fed. Cir. 1998)). Indeed, "whether a claim is invalid under § 101 'is a matter of both claim construction and statutory construction.'" *Id.* (characterizing and quoting *State St.*, 149 F.3d at 1370). The Federal Circuit recently observed that:

> Although Ultramercial has since been vacated by the Supreme Court, we perceive no flaw in the notion that claim construction is not an inviolable prerequisite to a validity determination under § 101. *We note, however, that it will ordinarily be desirable—and often necessary—to resolve claim construction disputes prior to a § 101 analysis, for the determination of patent eligibility requires a full understanding of the basic character of the claimed subject matter.*

Bancorp Servs., L.L.C. v. Sun Life Assur. Co. of Canada, 687 F.3d 1266, 1273-1274 (Fed. Cir. 2012) (emphasis added). Defendants' conclusory statements about the scope of the various claims of the '342 Patent [*see* Motion, pp. 1-2] again do not satisfy Defendants' burden of

persuasion or proof. Defendants' Motion must also be denied for this reason alone.

D. The '342 Patent Claims Patent Eligible Subject Matter

Though Defendants' Motion should be denied for all of the deficiencies explained above, GTG now addresses Defendants' allegation that the '342 Patent claims are patent ineligible. In reality, an examination of exemplary claims of the '342 Patent illustrate patent eligibility under 35 U.S.C. § 101.

1. Claims 1 and 9 Recite Patent Eligible Inventions

Claim 1 of the '342 Patent recites three steps. A sample from a human is "analyzed" to detect the presence of one or more genetic variations in the ACTN3 gene, the presence of two 577R alleles are "detected" in the ACTN3 gene, and the information gathered in the first two steps is then used to "predict" the potential sprinting, strength or power performance of the human. [Ashdown Dec., ¶ 4.] Contrary to Defendants assertion [Motion, p. 5], the prediction step of Claim 1 is more than a mental step. The dictionary definition of "predict" is to "declare or indicate in advance" or "to say that something will happen in the future" [*Id.* at ¶¶ 8-9.] Thus, the prediction step *requires the act* of declaring or stating the potential sprinting, strength or power performance of the human. [*Id.* at ¶ 4.]

Claim 9 recites similar limitations to Claim 1, and adds an additional step of "selecting" a training program based on predicted potential sprinting, strength and power performance of the predicting step. [*Id.* at ¶ 7.] Claim 9 thus not only requires the act of predicting the potential sprinting, strength or power performance of the human, but also *requires the act* of selecting a training program selected based on the prediction. [*Id.*]

The steps of Claims 1 and 9, taken as a whole,[4] recite specific applications and are therefore patent eligible. *See, e.g., PerkinElmer*, 2012 U.S. App. LEXIS 23845 at *16-17 n.2 ("the claims . . . require the further act of immunization in accordance with a lower-risk schedule, thus moving from abstract scientific principle to specific application.").

2. Patents Issued After *Mayo* Evidence Patent Eligibility

The United States Patent and Trademark Office ("USPTO") on July 3, 2012, issued internal guidelines for analyzing patent eligibility of claims in accordance with the *Mayo* decision. [Ashdown Dec., ¶ 10.] Since then, the USPTO has allowed numerous patents to issue with claims having combinations of process steps like Claim 1 of the '342 Patent. For example, U.S. Patent No. 8,354,229 entitled "MiR-25-based Methods for the Diagnosis and Prognosis of Acute Myeloid Leukemia" issued on January 1, 2013 ("the '229 Patent"), U.S. Patent No. 8,349,555 entitled "Methods and Compositions for Predicting Death From Cancer and Prostate Cancer Survival Using Gene Expression Signatures" issued on January 8, 2013 ("the '555 Patent"), and U.S. Patent No. 8,383,089 entitled "Use of IMP3 as a Prognostic Marker for Cancer" which issued on February 26, 2013 ("the '089 Patent"). [*Id.* at ¶¶ 11-13.] The following chart compares Claim 1 of the '342 Patent to claims from these patents:

The '342 Patent Claim 1	**The '229 Patent Claim 6**	**The '555 Patent Claim 1**	**The '089 Patent Claim 1 and 3**
A method to predict potential sprinting,	A method of determining the	A method for predicting a clinical	A method for treating a subject having renal cell

[4] The Supreme Court has counseled against Defendants' piecemeal analysis of individual claim limitations. [*See* Motion, pp. 4-6.] "In determining the eligibility of respondents' claimed process for patent protection under section 101, *their claims must be considered as a whole*. It is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis. This is particularly true in a process claim because a new combination of steps may be patentable even though all the constituents of the combination were well known and in common use before the combination was made." *Research Corp. Techs. v. Microsoft Corp.*, 627 F.3d 859, 869 (Fed. Cir. 2010) (quoting *Diamond v. Diehr*, 450 U.S. 175, 188 (1981) (emphasis added).

strength, or power performance in a human comprising:	prognosis of a subject having, or suspected of having acute myeloid leukemia, comprising:	outcome for a human subject having prostate cancer, comprising:	carcinoma (RCC), comprising the steps of:
a) *analyzing a sample obtained from the human* for the presence of one or more genetic variations in α-actinin-3 (ACTN3) gene;	*obtaining a test sample from subject* having, or suspected of having AML, wherein the sample is extracted from at least one of: blood, bone marrow, and tissue suspected of having leukemic cells, measuring, by hybridization assay, the level of at least one miR gene product of miR-25 in a test sample from said subject,	*determining the mRNA expression of a set of genes in a sample from the human* subject having prostate cancer, wherein the set of genes consists of the following 11 genes GBX2, MK167, CCNB1, BUB1, KNTC2, USP22, HCFC1, RNF2, ANK3, FGFR2, and CES1, and	(a) *obtaining from the subject a primary tumor tissue of the kidney*;
b) *detecting the presence of two 577R alleles* at the loci encoding amino acid number 577 of the α-actinin-3 (ACTN3) protein; and	*comparing the level of miR-25 gene product in the test sample* relative to a control level of miR-25 gene product,	*determining the stem cell-resembling phenotype association index ("SPAI") for the set of genes in the sample* by comparison of the mRNA expression of each of the 11 genes from the human subject having prostate cancer to each of the 11 genes in a reference sample from a stem cell, wherein said stem cell is a peripheral nervous system neurosphere;	(b) *determining the presence or level of IMP3 in a primary tumor* and

c) *predicting the potential sprinting, strength, or power performance of the human*, wherein the presence of two copies of the 577R allele is positively associated with potential sprinting, strength, or power performance.	and *predicting the subject's prognosis*, wherein: the miR-25 gene product is associated with an adverse prognosis in AML; and an increase in the level of the at least one miR-25 gene product in the test sample, relative to the level of a corresponding miR-25 gene product in the control, is indicative of an adverse prognosis.	wherein a subject whose sample has a positive SPAI is *predicted to have a poor clinical outcome* and a subject whose sample has a negative SPAI is *predicted to have a good clinical outcome*.	(c) treating the subject for metastasis if the primary tumor expresses IMP3.
			3. The method of claim 1, further comprising determining at least one other factor, the presence, absence or level of which reasonably correlates with the *prediction of the prognosis of the subject*.

The USPTO has even recently issued patents with claims like Claim 1 of the '342 Patent to Stanford University.[5] For example, U.S. Patent No. 8,361,723 entitled "Keratin 8 Mutations are Risk Factors for Developing Liver Disease of Multiple Etiologies" issued January 29, 2013 ("the '723 Patent"), U.S. Patent No. 8,309,316 entitled "Methods and Compositions for Risk Stratification" issued November 13, 2012 ("the '316 Patent"), and U.S. Patent No. 8,296,076 entitled "Noninvasive Diagnosis of Fetal Aneuploidy by Sequencing" issued October 23, 2012 ("the '076 Patent"). [Ashdown Dec., ¶¶ 15-17.] The following chart compares Claim 1 of the '342 Patent to claims from these Stanford University patents:

The '342 Patent Claim 1	**The '723 Patent Claim 1**	**The '316 Patent Claim 1**	**The '076 Patent Claim 1**
A method to predict potential sprinting, strength, or power performance in a human comprising:	A method for detecting a predisposition to liver disease in a human, the method	A method of profiling a first cell population, said method comprising:	A method of testing for an abnormal distribution of a chromosome in a sample comprising a

[5] Defendants' counsel Mark Lemley is the William H. Neukom Professor of Law, and Director of the J.D. and L.L.M. programs in Law, Science and Technology at Stanford University. [Ashdown Dec., Ex. A at ¶ 14.]

	comprising:		mixture of maternal and fetal DNA, comprising the steps of:
a) *analyzing a sample obtained from the human* for the presence of one or more genetic variations in α-actinin-3 (ACTN3) gene;	*obtaining a biological sample from a human*, and *analyzing* the biological sample for the presence or absence of one or more mutations in a keratin K8 protein tail domain selected from the group consisting of G433S, R453C, and a combination of any of the foregoing, and	*contacting each of a first cell population and at least one second cell population with at least two distinguishably detectable activation state-specific binding elements,* wherein each said activation state-specific binding element is specific for a state of a signaling node in a cell of said first cell population and a cell of said second cell population;	(a) *obtaining maternal and fetal DNA from said sample;*
b) *detecting the presence of two 577R alleles* at the loci encoding amino acid number 577 of the α-actinin-3 (ACTN3) protein; and	*detecting a predisposition to liver disease* based on the presence of the one or more mutations.	*detecting the level of binding* of said at least two distinguishably detectable activation state-specific binding elements to their corresponding signaling node state in each of said cell populations to determine the state of each of said signaling nodes in each of said cell populations; *comparing* the state of each of said signaling nodes in said first cell population with the state of each of said signaling nodes in said at least one second cell	(b) *sequencing predefined subsequences of the maternal and fetal DNA* to obtain a plurality of sequence tags aligning to the predefined subsequences, wherein said sequence tags are of sufficient length to be assigned to a specific predefined subsequence, wherein the predefined subsequences are from a plurality of different chromosomes, and wherein said plurality of different chromosomes comprise at least one first chromosome suspected of having an abnormal distribution in said

		population; and	sample and at least one second chromosome presumed to be normally distributed in said sample; (c) assigning the plurality of sequence tags to their corresponding predetermined subsequences; (d) determining a number of sequence tags aligning to the predetermined subsequences of said first chromosome and a number of sequence tags to the predetermined subsequences of the second chromosome; and
c) *predicting the potential sprinting, strength, or power performance of the human*, wherein the presence of two copies of the 577R allele is positively associated with potential sprinting, strength, or power performance.		*producing a profile* of said first cell population based on said comparison of the state of each of said signaling nodes in said first cell population to the state of each of said signaling nodes in said second cell population.	(e) *comparing the numbers from step (d) to determine the presence or absence of an abnormal distribution of said first chromosome.*

These examples of the USPTO's recently issued claims demonstrate that Claim 1 of the '342 Patent is patent eligible under 35 U.S.C. § 101 in view of *Mayo*.

E. The '342 Patent Claims Are Patentable Under the Machine-Or-Transformation Test

Under the machine-or-transformation test, a claimed method qualifies as statutory subject matter if: "(1) it is tied to a particular machine or apparatus, or (2) it transforms a particular

article into a different state or thing." *Bilski v. Kappos*, 130 S. Ct. 3218, 3225-26 (2010) (quoting *In re Bilski*, 545 F.3d 943, 954 (Fed. Cir. 2008)). The test assists in the evaluation of whether a method claim would improperly "pre-empt substantially all uses of [a] fundamental principle if allowed," because "[a] claimed process involving a fundamental principle that uses a particular machine or apparatus would not pre-empt uses of the principle that do not also use the specified machine or apparatus in the manner claimed." *In re Bilski*, 545 F.3d at 954. Similarly, "a claimed process that transforms a particular article to a specified different state or thing by applying a fundamental principle would not pre-empt the use of the principle to transform any other article, to transform the same article but in a manner not covered by the claim, or to do anything other than transform the specified article." *Id.*[6]

1. Exemplary Claims 1 and 9 Are Transformative

The prediction steps of Claim 1 and 9 require transformation of the information obtained in prior steps of analyzing and detecting into a prediction of potential sprinting, strength, or power performance. [Ashdown Dec., ¶¶ 4, 7.] Claims 1 and 9 are therefore transformative and patent eligible. *See Myriad*, 689 F.3d at 1333-34; *Bilski v. Kappos*, 130 S. Ct. at 3225-26, 3227.

2. Exemplary Claim 4 is Transformative

Claim 4 requires the use of an antibody to measure the amount of the ACTN3 protein. ['342 Patent, D.I. 1, Ex. A at 30:1-3.] Antibodies used for such measurements are man-made. [Ashdown Dec., ¶ 5.] In *Myriad*, the court found that the inclusion of the host cells with and without a potential cancer therapeutic made the claims patent eligible because the host cells involved an inherently transformative step. 689 F.3d at 1333-34. Claim 4 is akin to a host cell

[6] The Federal Circuit recently relied on the machine-or-transformation test in affirming the patent eligibility of a claimed method for screening potential cancer therapeutics in *Myriad*. 689 F.3d at 1333-34.

used to measure the efficacy of a cancer therapeutic. Antibodies are man-made as they are made using a foreign mammal or synthetically synthesized. [Ashdown Dec., ¶ 5]. Antibodies work by attaching to a site location specific to an antigen, in this case the ACTN3 protein, to form an antibody-antigen complex. [*Id.*] This antibody-antigen complex or the use of the antibody-antigen complex is not found in nature since the antibody is man-made through either the use of a foreign mammal or synthetically. [*Id.*] Claim 4 is also transformative and patent eligible. *See Myriad*, 689 F.3d at 1333-34*; Bilski v. Kappos*, 130 S. Ct. at 3225-26, 3227.

3. Exemplary Claim 6 Includes Both Machine and Transformation

Claim 6 requires an identification of the 577R alleles in the human's genomic DNA using DNA sequencing, allele-specific hybridization, allele-specific amplification or restriction fragment length polymorphism analysis. ['342 Patent, D.I. 1, Ex. A at 30:7-11.] Each of these analysis methods, with the possible exception of RFLP, require the use of DNA amplification and therefore create isolated, man-made DNA sequences. [Ashdown Dec., ¶ 6.] Moreover, each of these analysis methods require the use of various machines. [Ashdown Dec., ¶ 6.] Claim 6 thus satisfies both the machine and transformation tests and is patent eligible. *Myriad*, 689 F.3d at 1333-34.

F. The '342 Patent Is Akin To Valid "Guidepost" Patents

The '342 Patent is like other "guidepost" patents upheld as reciting statutory subject matter. For example, in the English case *Neilson v. Harford*—discussed by the Supreme Court in *Prometheus*—the patent-in-suit claimed a device with a receptacle for pre-heating air destined for a fire or furnace. *O'Reilly v. Morse*, 56 U.S. 62, 114-15 (1854) (quoting *Neilson v. Harford*, Webster's Patent Cases); *see Mayo*, 132 S. Ct. at 1300. When the patent was challenged as claiming an unpatentable principle (i.e. "that hot air will promote the ignition of fuel better than cold"), the *Neilson* court acknowledged that "[i]t is very difficult to distinguish [the patent-in-

suit] from the specification of a patent for a principle." *O'Reilly*, 56 U.S. at 115-16 (quoting *Neilson*). The claimed process was deemed patentable because it "did more than simply instruct users to use the principle that hot air promotes ignition better than cold air, since it explained how the principle could be implemented in an inventive way." *Mayo*, 132 S. Ct. at 132.

Similarly, in *Diamond v. Diehr*, the USPTO had rejected, as patent-ineligible, claims for a process of curing rubber in a heated mold, because "in several steps of the process a mathematical equation and a programmed computer are used." 450 U.S. at 180-81, 185. The *Diehr* claims required determining the temperature of the rubber curing mold at frequent intervals during a curing process, and inputting that temperature into the Arrhenius equation to repeatedly calculate (using a computer) the required curing time. *Id.* at 177-78, 180-81 & n.5. The claims also recited steps for curing rubber, such as loading a heated mold with rubber for curing, and removing the cured rubber from the mold. *Id.* at 181 n.5. Affirming the patentability of the claims, the Supreme Court reasoned that "[Respondents] seek patent protection for a process of curing synthetic rubber. Their process admittedly employs a well-known mathematical equation, but they do not seek to pre-empt the use of that equation. Rather, they seek only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process." *Id.* at 187. The Supreme Court explained that as long as "a claim containing a mathematical formula implements or applies that formula in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect (*e.g.*, transforming or reducing an article to a different state or thing), then the claim satisfies the requirements of § 101." *Id.* at 192.

Likewise, the '342 Patent claims require one to analyze the ACTN3 gene and the detection of two 577R alleles in the protein in order to predict the potential sprinting, strength or

power performance of the human when the alleles are present. [Ashdown Dec., ¶ 4.] In order to detect the two 577R alleles, the human sample must be analyzed using a machine to isolate the DNA (i.e., a machine and transformation) to detect the presence of the alleles (i.e., by applying the discovery). [Ashdown Dec., ¶¶ 4-7.] The '342 Patent claims a "process which, when considered as a whole, is performing a function which the patent laws were designed to protect." *Diamond*, 450 U.S. at 192. The '342 Patent is thus akin to the "guidepost" claims found patent eligible in *Neilson* and *Diehr*.

III. CONCLUSION

As explained above, Defendants' Motion is both facially deficient and lacks merit. GTG respectfully requests that the Court deny the Motion.

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BENESCH, FRIEDLANDER, COPLAN & ARONOFF LLP

By: */s/ Raymond H. Lemisch*

Raymond H. Lemisch, Esquire (No. 4204)
222 Delaware Avenue, Suite 801
Wilmington, DE 19801
(302) 442-7008 Telephone
(302) 442-7012 Facsimile
rlemisch@beneschlaw.com

- and -

Robert R. Brunelli, Esquire
rbrunelli@sheridanross.com
Benjamin B. Lieb, Esquire
blieb@sheridanross.com
SHERIDAN ROSS P.C.
1560 Broadway, Suite 1200
Denver, Colorado 80202-5141
(303) 863-9700
(303) 863-0223 (facsimile)
litigation@sheridanross.com

Attorneys for Plaintiff Genetic Technologies Limited

7575597 v1